Working With Stakeholders on Scientific Opportunities for Biologics Products

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www.fda.gov/oc/initiatives/criticalpath.htm

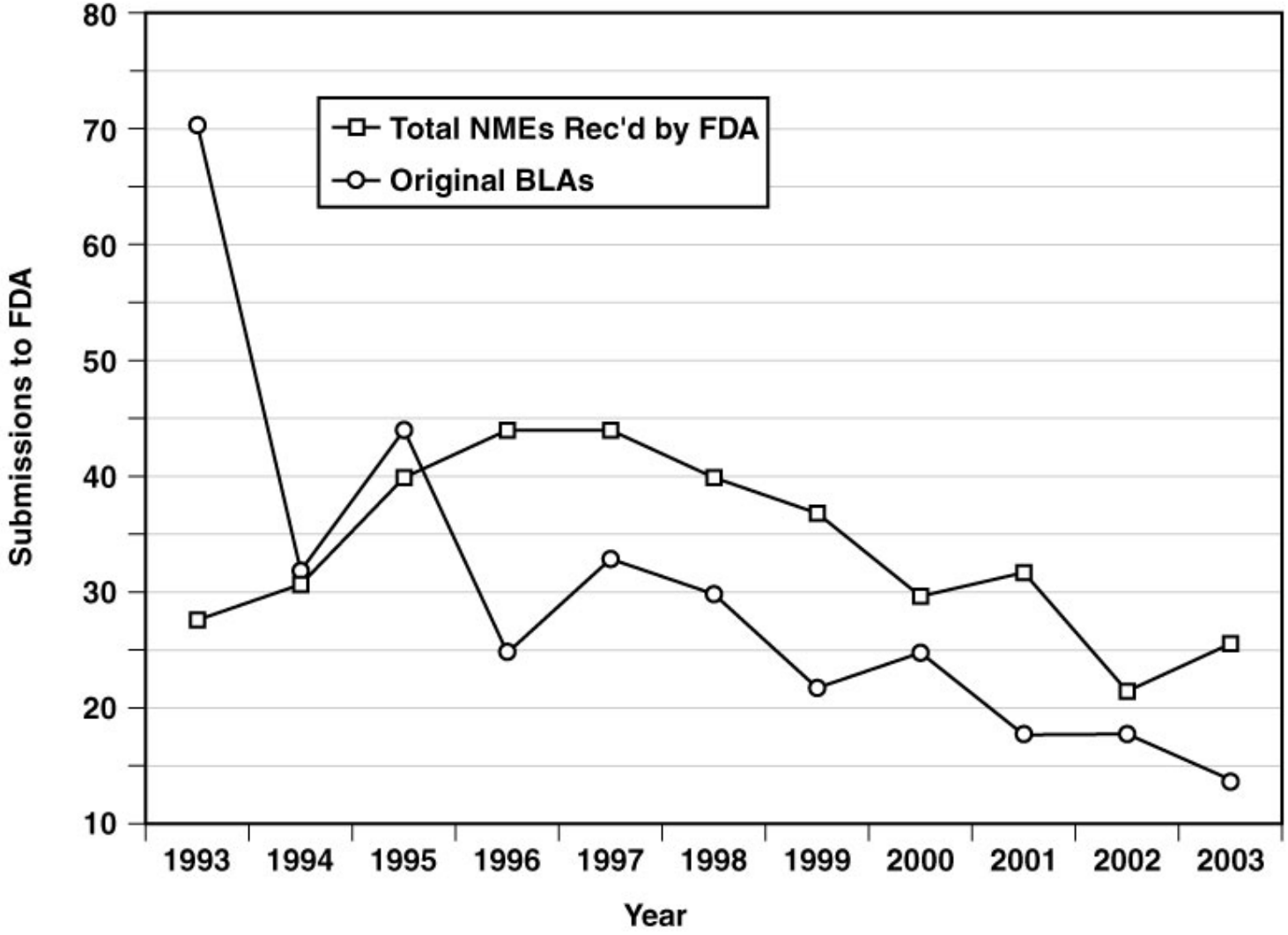
Innovative Technology Advancing Public Health

CBER: Vision & Mission

Vision: To use sound science and regulatory expertise to: Protect and improve public and individual health in the US and, where feasible, globally and facilitate the development, approval and access to safe and effective products and promising new technologies

Mission: To ensure the safety, purity, potency, and effectiveness of biological products…for the prevention, diagnosis, and treatment of human diseases, conditions or injury, including helping to defend the public against the threats of emerging infectious diseases and bioterrorism

Figure 2: 10-Year Trends in Major Drug and Biological Product Submissions to FDA



Tomorrow's Medical Breakthroughs

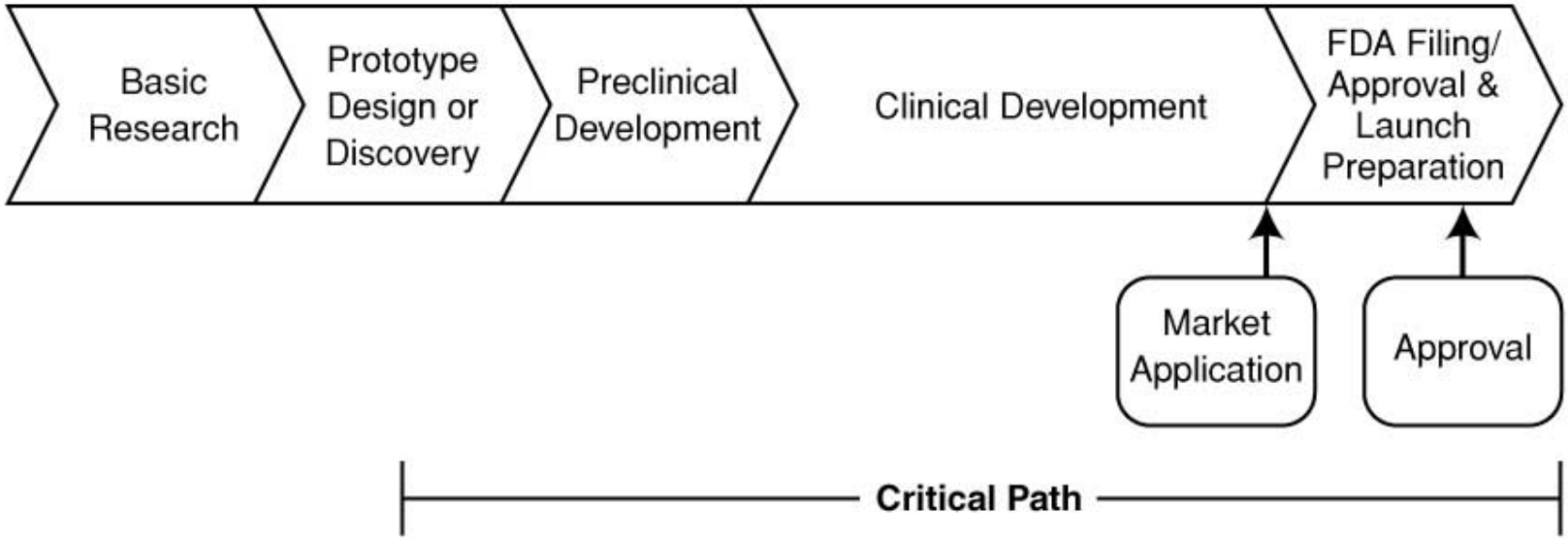
- Many serious diseases afflict our population and are waiting for better treatments: autism, Alzheimer's disease, AIDS, cystic fibrosis, heart disease, diabetes, morbid obesity, multiple sclerosis, muscular dsytrophy, rheumatoid arthritis, osteoarthritis, systemic lupus, schizophrenia, stroke, and many more

Question: How do we work with our stakeholders to develop an agenda to facilitate medical breakthroughs becoming treatment realities?

FDA Critical Path Initiative

- Facilitate product development through better tools and latest technologies for safety, efficacy and product manufacturing
  www.fda.gov/oc/initiatives/criticalpath.html
- Focus intramural and extramural science as resources permit
  - » Identify areas, e.g., new technologies in need of standards, methods, assays, guidance
  - » Special unmet needs and opportunities for impact where economic incentives may be uncertain and/or private sector resources may be limited or otherwise focused – e.g. product meeting emerging public health needs, new technologies
  - » Identify cross-cutting "roadblocks", scientific and regulatory, and develop appropriate solutions
  - » Guidance, standards, outreach, creative approaches to product development, safety/efficacy assessment and review, consistent production

Figure 4: The Critical Path for Medical Product Development



Three Dimensions of the Product Development Science: Going Beyond Discovery and Invention

- **Assessment of Safety** – how to predict if a potential product will be harmful?
  - Preclinical assays
  - Clinical trial design
- **Proof of Efficacy** -- how to determine if a potential product will have medical benefit?
  - Biomarkers, e.g., Surrogate markers of efficacy
- **Industrialization** – how to manufacture a product at commercial scale with consistently high quality?
  - Predict "scale up" problems early
  - Quality: Standards & Assays

Product Development Science Is Underdeveloped

- Falls outside traditional areas of research and federal funding (e.g., product discovery).
  - Development = Assays, standards, relevant biomarkers, animal models for safety & efficacy testing
- Currently using 20th century tools to predict performance and assess manufacturing quality of 21st century products.

Why focus on the science of product development?

- *Generally targets unmet needs with regulatory implications to facilitate the development of products*
  - Benefits multiple sponsors; communication
- Maintains staff "cutting edge" expertise needed for dealing with evolving biotechnologies
  - Scientific expertise and confidence foster objectivity
    - » Reduces risks of reflexive over- or under-protectiveness
    - » Make regulation more scientific, less "defensive"

Proposal: CBER Proactively Improving the Product Development Process

- Work with stakeholders to develop and prioritize needs for scientific tools and knowledge
- Coordinate CBER staff, academic, and industry scientists to develop the science needs
- Apply new science to chart a more predictable and efficient path for new biologics product evaluation
- Assess progress and revise priorities in collaboration with stakeholders on a routine basis

Vision for Innovative Biologics Product Science

- Get more innovative products to patients.
- Achieve robust product development pathways that are efficient and predictable.
  - Many promising biologics products have no established development pathways, e.g., gene and cell therapies
- Develop new scientific toolkits that bring scientific advances into the product development process.
- Perform research on tools that remove specific identified obstacles in product development.

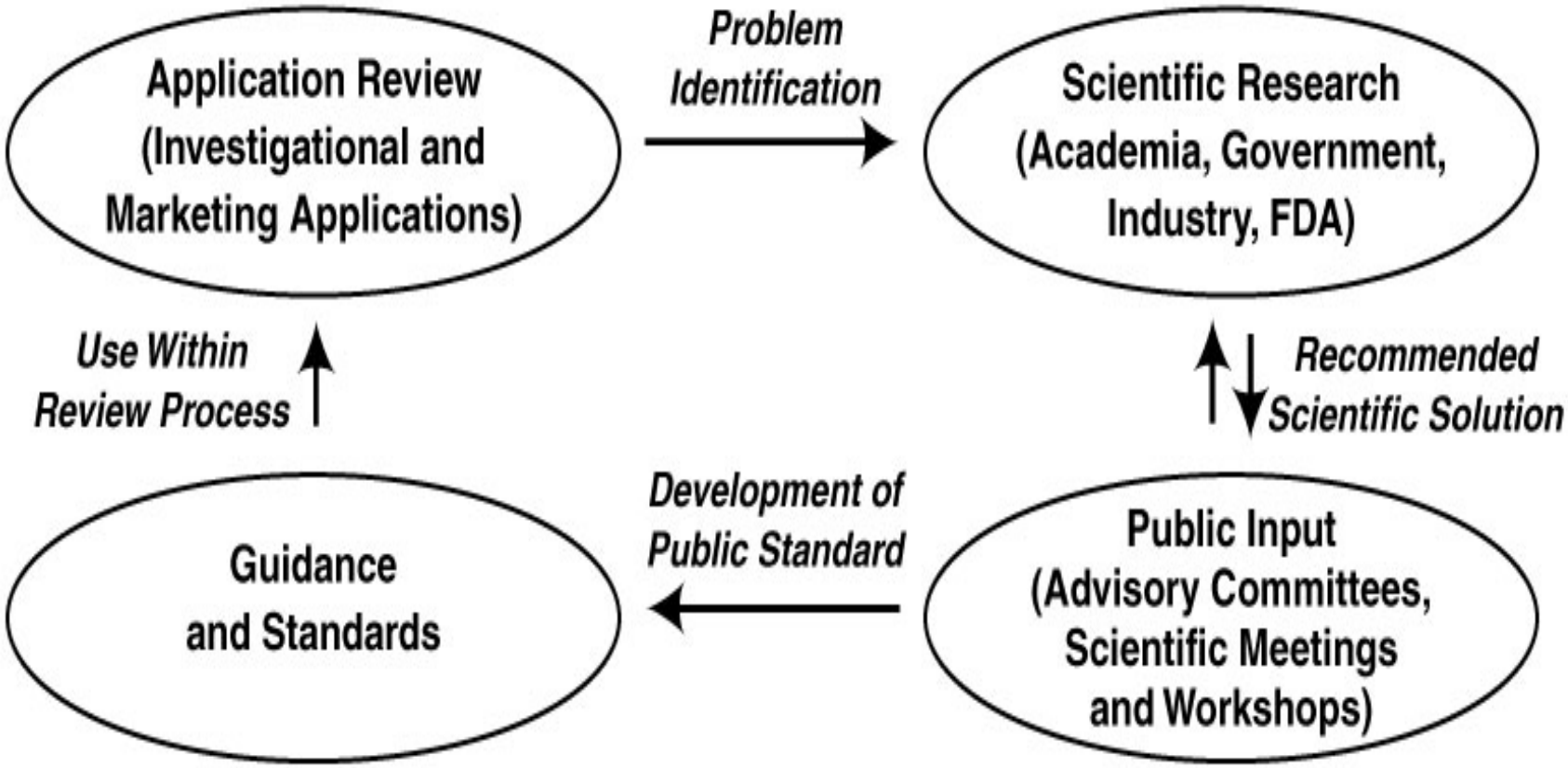
Improving Predictability for Biologics Product Development: Outcomes

- Reduce cost by identifying and focusing resources on the best candidate products early in development
- Makes product evaluation more quantitative, consistent, predictable
- Chart a clear pathway and process for incorporating new scientific approaches into the study and manufacture of new products

Why CBER? Unique Role of the Center vis-a-vis Science of Biologics Product Evaluation

- Innovators create critical path tools that are typically applicable to their specific products and not shared with others in industry
- CBER scientists are part of the review process during product development--they see the successes, failures, and missed opportunities
- CBER guidance documents that are based on science can foster innovation and improve chances of success.
- CBER can play a convening and coordinating role for scientific needs across sponsors

Figure 8: Problem Identification and Resolution During the FDA Product Review Process



Selected Regulatory Accomplishments of Product Development Science

- **Public Health**
  - WNV Blood Donor Screening initiated in 8 months, new HIV, Hep C tests, TRANSNET Supply Monitoring Pilot
  - Successful response to “white particles” in blood for transfusion, SARS, other EID events: including outreach on product development
  - Risk Assessment/Guidances re: TSE, CT & blood safety
  - New products, e.g. tD, Flumist vaccine

Selected Regulatory Accomplishments of Product Development Science

- **New Technologies**
  - Successful management of SCID/Gene Therapy adverse events
    - » Leukemia in SCID-X gene therapy recipients in France
    - » Death of patient following adenovirus vectored gene therapy in US
  - BRMAC re: Development of islet cell transplantation
  - Outreach/international activities in gene therapy/xenotransplantation
  - Cell Substrate Guidance
  - Major research on GT and xenotransplantation safety, stem cell characterization, CT products and assays

Today's Opportunities

- Brief overview of CBER product responsibilities, current science and future possibilities
- Bring together industry, academia, patient advocacy groups and others to present/discuss their issues and priorities for biologics product science opportunities
- Open discussion of scientific opportunities by participants and CBER staffs

Where do we go from here?

- **Today's discussions will be summarized, published and used to:**
  - **Develop future CBER science priorities and agenda**
  - **Seek outside scientists for consultation, collaborative projects or to inspire for independent projects**
- **Transparency of process:**
  - **CBER product Office science organization and outcomes to be presented and reviewed in public meetings in 2005**
  - **Continue regular reviews of CBER science programs to maintain momentum and update priorities**
- **Scientific advances to be communicated in Guidances, policy and publications**

Thanks!

- *We believe that FDA can help identify opportunities and develop better tools to improve the safety, efficacy and predictability of product development along the "critical path" to patients*
- *We look forward to continuing engagement with colleagues and stakeholders in academia, industry, and the public both to further identify and target areas for scientific investment*
- *Together we can enhance successful product development that promotes individual and public health*

CBER: INNOVATIVE TECHNOLOGY ADVANCING PUBLIC HEALTH